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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/594,964 | 09/29/2006 | Tomoki Todo | 042715-5024 | 1879 |

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| EXAMINER | |
|---|---|
| SALIMI, ALI REZA | |
| ART UNIT | PAPER NUMBER |
| 1648 | |
| MAIL DATE | DELIVERY MODE |
| 04/20/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/594,964 | TODO, TOMOKI | |
| | Examiner | Art Unit | |
| | A R. Salimi | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 April 2009*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *17-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Request Continued Examination (RCE)*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/06/2009 has been entered.

### *Response to Amendment*

This is a response to the amendment filed on 10/03/2008. Claims 1-16 have been canceled. New claims 17-27 have been added and are currently pending.

Please note any ground of rejection that has not been repeated is removed. Applicant's response deemed persuasive.

**New Grounds of Rejection**:

### *Claim Rejections - 35 USC § 112*

Claims 17-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cancer utilizing HSV vector wherein gamma34.5 gene, ICP6 gene, and ICP47 gene are deleted or inactivated , does not reasonably provide enablement for all types of HSV vectors to be utilized in treating cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The current scope of the claims, in particular independent claims, is directed to all types of HSV vectors. Applicants have general statements regarding the broad class of HSV vectors, however, the examples have

utilized what is already well known and well disclosed in the art. No general HSV expression vector has been taught that would enable the full scope of the now claimed invention. And with regard to an unpredictable field, this does not constitute an adequate disclosure. See Fiers v. Revel, 984 F.2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993); and also decision by the Federal Circuit with regard to the enablement issues see Genentech Inc. v. Novo Nordisk, 108 F.3d 1361, 42 USPQ2d 1001 (Fed. Cir. 1997). For example, the CAFC stated that "It is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute enablement." (See page 1005 of the decision). In the instant case the specification does not teach or provide any guidance for employment of all types of HSV vectors. This means the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. See In re Wright, 999 F.2d 1557,1562, 27USPQ2d 1510, 1513 (Fed. Cir. 1993).

The disclosure must adequately guide the art worker to determine, without undue experimentation. Applicant cannot rely on the knowledge of those skilled in the art to enable the claims without providing adequate teaching. Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim. Many of these factors have been summarized In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a **written description** of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession** of the claimed invention. In the instant disclosure, Applicant has only disclosed one HSV vector having deletion or inactivation in gamma 34.5, ICP6, and ICP47 genes. No other vectors were disclosed. Therefore, a written description of the other claimed HSV vectors should be disclosed to overcome this rejection. See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. 35 USC 112 requires inter alia that a patent specification contain a written description of the invention and the manner and process of making and using it "in such full clear and concise terms as to enable one skilled in the art ... to make and use" the invention. Case law has made it clear that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question,

the "written description" requirement has not been met even though the description may be enabling.

See *University of California v. Eli Lilly*, 19 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al (WO 02/076216 A1) and Hara et al (Cancer Gene Therapy, 2000, Vol. 7, pages 83-90).

Johnson et al disclosed a herpes virus expression vector wherein ICP47 and gamma 34.5 regions are inactivated (see claims 4, 28). Moreover, they disclosed insertion of gamma-interferon (see Column 4, paragraph[0033]. In addition, they taught inactivation of ICP6 region as well (See claim 5). They also taught the method of utilizing the vector in inducing immune response (see claims 6-8). In addition, they taught expression of all types of cytokines (see page 10, lines 30). This only differs since they did not disclose co-administration of IL-18 and IL-12.

Hara et al taught utilization of both IL-12 and IL-18 showed synergistic efficacy against tumor and taught systemic administration of IL-18 and local expression of IL_12 enhanced the antitumor efficacy (see the abstract, and page 89, last paragraph).

Therefore, it would have been obvious for one of ordinary skill in the art to co-administer both IL-12 and IL-18 as taught by Hara et al into expression vector taught by Johnson et al to induce an enhancing response against neoplasia. Johnson had already taught insertion of gamma-interferon. As Applicant is aware, IL-18 induces gamma-interferon. Hence, in essence Johnson's product achieves the same task. Still further, one of skilled in the art being familiar with the above cited teaching at the time the invention was filed would not have anticipated any unexpected results. Here, the prior art provides the teaching as to the appropriate vector, and the cytokines that lend themselves to enhanced activity. The art suggest that combination of IL-12 and IL-18 is beneficial in treating tumors. The art even taught expression of IL-12, and

systematic administration of IL-18 provides synergy without the added drawbacks, i.e. toxicity. Therefore, one would have been motivated by the above cited art to induce a synergistic effect against cancer cells utilizing the HSV vector as taught by Johnson and co-administer the IL-18 and IL-12, because utilizing similar methods familiar to those ordinary skilled in the art is deemed obvious, In re Kubin (Fed. Cir. 2009).

Applicants are reminded that the combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results. See KSR Int'l Co. v. Teleflex Inc., 550 U.S. (2007). Thus, the invention as a whole is deemed prima facie obvious absent any unexpected results.

No claims are allowed.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to A. R. Salimi whose telephone number is (571) 272-0909. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. The Official fax number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/A R Salimi/
Primary Examiner, Art Unit 1648

04/17/2009